

Factors Associated With Postoperative Infection After Percutaneous Nephrolithotomy

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Numerous studies have investigated risk factors for the development of postoperative infection in percutaneous nephrolithotomy (PCNL) patients. Herein, we describe our meta-analysis of the risk factors for the prediction of post-PCNL infectious complications. We searched electronic databases using a combination of the terms *percutaneous nephrolithotomy*, *risk factors*, *infection*, and *sepsis*. The primary outcome was post-PCNL infection as defined by fever $>38^{\circ}\text{C}$ or sepsis as defined by the Sepsis Consensus Definition Committee. Risk factors for infection in each study were identified and included for analysis if present in at least two studies. We used quantitative effect sizes in odds ratio to assess each endpoint. After application of criteria, 24 studies were found, of which 12 were prospective and 12 were retrospective. Of the prospective studies, preoperative urine culture, renal pelvis culture, stone culture, number of access points, hydronephrosis, perioperative blood transfusion, and struvite stone composition were found to be significantly associated with postoperative infection. Of the 12 retrospective studies, preoperative urine culture, stone cultures, number of access points, blood transfusion, stone size, and staghorn formation were associated with infection. Preoperative urine culture, stone culture, number of access points, and need for blood transfusion were consistently found to be significant factors. This indicates that the presence of bacteria in the urine/stone preoperatively as well as the amount of trauma the kidney sustains during the procedure are major predictors of postoperative infection.

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KEY WORDS

Nephrolithiasis • Percutaneous nephrostomy • Lithotripsy • Urinary tract infection

Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure designed to remove large-volume upper urinary tract stones. It is extremely effective yielding high stone-free rates.¹ However, significant complications can occur, including infection. In PCNL patients, postoperative sepsis has been reported in 0.3% to 7.6% of cases.²⁻⁴ Antibiotic prophylaxis has been recommended for patients subjected to PCNL to avoid infectious complications, as profiled in an American Urological Association (AUA) Best Practice Policy Statement.⁵ However, despite the use of antibiotics, sepsis remains the most common cause of perioperative mortality in these procedures.^{2,6} There have been numerous studies investigating potential risk factors for the development of postoperative infection in PCNL patients. From the studies, important perioperative factors, such as preoperative urine culture, and intraoperative stone and collecting system urine cultures, have been identified as predictors of infection.⁷⁻⁹ However, to our knowledge, there has not been a systematic meta-analysis assessing the findings from these studies. Herein, we describe our meta-analysis of the risk factors for the prediction of post-PCNL infectious complications.

Methods

Literature Search and Article Selection

This study was performed according to the criteria as listed in "Meta-analysis of Observational Studies in Epidemiology."¹⁰ The electronic databases PubMed, Scopus, and Ovid were searched using a combination of the medical subject heading terms *percutaneous nephrolithotomy*, *risk factors*, *infection*, and *sepsis*. From these searches,

102 studies resulted. Criteria for inclusion in this study included full-length original articles published in a peer reviewed journal; study population consisting of adults (>18 y); clearly identified comparison groups; the use of prophylactic antibiotic at time of anesthesia induction; treatment of patients with positive preoperative urine culture results until a negative culture result was obtained; studies reporting quantitative effect sizes in odds ratio (OR) with 95% CI relating to primary outcome or studies reporting actual numbers of the patients with and without risk; and the event rates in each group that could be used for calculation of OR. After application of these criteria, 24 studies met them, of which 12 were prospective and 12 were retrospective. The primary outcome was the development of post-PCNL infection as defined as fever with body temperature of >38°C or sepsis as defined by the Sepsis Consensus Definition Committee with two or more of the following conditions: (1) temperature <36°C or temperature >38°C, (2) heart rate >100 beats/min, (3) respiratory rate >20 breaths/min, and (4) leukocyte count >12,000 leukocytes/mL or <4000 leukocytes/mL.¹¹

Study Characteristics

Data were extracted independently by one reviewer. Risk factors for infection in each study were identified and included for analysis if present in at least two studies. Factors identified include preoperative urine culture, intraoperative renal pelvic urine culture, stone culture, presence of preoperative hydronephrosis, the number of access points made during the procedure, the need for perioperative or postoperative blood transfusion, struvite stones, staghorn stone configuration, stone size, duration of procedure, presence of residual

stone postoperatively, previous PCNL on the ipsilateral side, and the sex, body mass index (BMI), age, and diabetic status of the patient.

Statistical Analysis and Bias Assessment

The reported univariable OR for each risk variable was pooled between studies. When the univariable OR was not reported, the OR and 95% CI were calculated from the actual number of patients in the groups with and without risk and the event rates in each group. The calculated risk estimation of individual risk variables was then pooled into a combined analysis using random effects models to determine overall risk profile. Heterogeneity between studies was incorporated into the random effects model through the DerSimonian and Laird method. Heterogeneity was measured by Cochrane's Q statistic and I^2 score, and was considered significant if $P < .05$ (Q-statistic) or $I^2 > 30\%$ (I^2 score). Publication bias was assessed visually by funnel plots of effect estimates and by use of Egger's test; this bias was considered significant if $P < .05$. Statistical analysis was performed with Stata with two-tailed $P < .05$ considered significant.

Results

The search strategy ultimately yielded 28 articles. However, four articles were removed due to a non-standard prophylactic antibiotic regimen. The remaining 24 articles were further subgrouped into prospective and retrospective study groups.

Prospective Studies

A total of 12 prospective studies with a total patient population of 1348 were included. Of these studies, the primary outcome in seven studies was systemic inflammatory response syndrome (SIRS), whereas five

studies used fever as the endpoint. Positive culture results were found to be significantly associated with postoperative infection, especially preoperative urine culture (effect size [ES] 2.14, 95% CI, 1.09-4.19; $P = .026$), intraoperative renal pelvis culture (ES 8.27, 95% CI, 3.03-16.98; $P = .0001$), and stone culture (ES 5.68, 95% CI, 2.66-11.85; $P = .0001$). Hydronephrosis (ES 0.38, 95% CI, 0.21-0.67; $P = .001$), number of access points (ES 3.61, 95% CI, 1.47-8.87; $P = .005$), perioperative blood transfusion (ES 2.25, 95% CI, 1.22-4.13; $P = .009$) and struvite stone composition (ES 3.33, 95% CI, 1.82-6.13; $P = .0001$) were also found to be significant. Of the significant factors, intraoperative renal pelvis urine culture was found to have the largest effect size. Heterogeneity was significant for preoperative urine ($I^2 = 52\%$; $P = .052$) and stone culture ($I^2 = 74.6\%$; $P < .0001$). For factors found to be significantly associated with postoperative infection, no publication bias was found through use of Egger's test.

Retrospective Studies

Twelve retrospective studies with a patient population of 3183 were included. Of these studies, the primary outcome of seven studies was SIRS, whereas it was fever in five. Preoperative urine culture (ES 2.03, 95% CI, 1.56-2.66; $P = .0001$) and stone cultures (ES 3.98, 95% CI, 1.97-8.08; $P = .0001$) were found to be significantly associated with infection; however, intraoperative renal pelvis urine culture ($P = .194$) was

characteristics were found to be significantly associated with infection, such as stone size (0.304, 95% CI, 0.12-0.48; $P = .001$), staghorn stone configuration (ES 1.88, 95% CI, 1.1-3.07; $P = .011$), and residual stone. Overall, stone culture had the largest effect size. Significant heterogeneity was present for stone culture ($I^2 = 74\%$; $P = .002$), transfusion ($I^2 = 55.5\%$; $P = .047$), number of access points ($I^2 = 76.9\%$; $P = .002$), and duration of procedure ($I^2 = 78.5\%$; $P < .0001$). For factors found to be significantly associated with postoperative infection, no publication bias was found through use of Egger's test.

Discussion

For patients with large renal stone burden, PCNL remains the procedure of choice. However the occurrence of complications is significant and ranges at a rate of 18.30% to 83%.^{1,4} Of these complications, infection remains a seminal event as sepsis is the leading cause of perioperative mortality.^{2,6} With sepsis established as an important complication of PCNL, focus has shifted to trying to predict its occurrence based on risk

pelvic urine culture, and stone culture have been indicated in literature as significant risk factors for infection.^{9,12} Furthermore, several studies have concluded that intraoperative cultures are more important in predicting postoperative infection compared with preoperative culture.^{8,12,13} These conclusions were supported by our meta-analysis of prospective studies, as all three factors were found to be significant. In addition, intraoperative renal pelvis and stone culture results were the strongest predictors of postoperative infection. In the retrospective analysis, both preoperative and stone cultures were significant; however, renal pelvis culture was not. This is likely due to the low number of retrospective studies (2) that included this factor.

Heterogeneity was significant for preoperative urine and intraoperative stone culture in the prospective studies. This was most likely due to the results of the study by Kumar and colleagues,¹⁴ which had a significantly higher effect size than the other studies. Without this study, the I^2 would have changed to 18.8% and 30% from 77.7% and 70.8%, respectively.

Perioperative factors, including blood transfusion and number of access points, were found to be significantly associated with infection in both the prospective and retrospective meta-analyses.

factors. There have been numerous studies investigating potential risk factors for the development of postoperative infectious complications in PCNL patients.

Perioperative factors, including blood transfusion and number of access points, were found to be significantly associated with infection in both the prospective and retrospective meta-analyses. Obtaining percutaneous access involves traumatic disruption of the urothelial lining potentially introducing bacteria/endotoxins into the bloodstream.¹⁵ More access points and requirement of blood transfusion could also be indications of an escalation of procedure complexity.

Preoperative urine culture, intraoperative renal pelvic urine culture, and stone culture have been indicated in literature as significant risk factors for infection.

not. Blood transfusion and number of access points, duration of procedure, and diabetic status of the patient were also significant. Stone

Urine cultures were the most common factors included in the reviewed studies. Preoperative urine culture, intraoperative renal

This could involve increased stone complexity or size, which are factors potentially associated with postoperative infection. Another indication of procedure complexity is duration of procedure, which was found to be significant in the retrospective but not in the prospective analysis.

Patient demographic factors were overall not associated with postoperative infection. Age, BMI, diabetes status, and sex were not found to be significant in our analysis of prospective studies. In the retrospective analysis, only diabetes was found to be significant. Of note, of the three studies that included diabetes, only one found it to be significant.¹⁶ The immune impairing effects of diabetes are well known, which can certainly be a predisposition to post-PCNL infection. However, a more informative factor would be serum glucose or hemoglobin A1c levels, as poor glucose control may be more of a contributing factor to infection than the diagnosis of diabetes itself. Although there are no studies on optimal glucose levels for PCNL procedures, guidelines for sepsis care report a target glucose level of ≤ 180 mg/dL

to be significant. Although BMI is often thought of as a risk factor

Preoperative hydronephrosis has also been investigated as a factor of

No studies in either the retrospective or prospective analyses found age or BMI to be significant.

for postoperative complications, the minimally invasive nature of PCNL may be a safeguard against this development.

Stone composition and characteristics were largely not significant in the prospective studies. Only struvite stone composition was found to be associated with postoperative infection. As the product of bacterial infection, struvite stones have been shown to harbor significant amounts of endotoxin. Stone manipulation can potentially cause release of these endotoxins promoting sepsis.¹⁹ Of interest is that staghorn stone formation was not significantly associated with infection. This may be due to such stones now predominantly being composed of hydroxyapatite and not struvite.²⁰ However, in the retrospective study analysis, stone size and staghorn stone configuration, and not struvite stone composition, were significantly associated with infection. By definition,

infection, although there is a lack of consensus as to its significance. Previous studies have theorized that preoperative hydronephrosis is associated with risk factors of infection, including large stone burden.¹⁴ Although hydronephrosis was found to be a significant factor in the prospective studies, the overall effect size was low at 0.382. This significance was likely driven by one study by Kumar and colleagues¹⁴ that contributed 51% of the total weight. This study was the only one, irrespective of retrospective/prospective design, to show significance. This suggests that hydronephrosis is either not significantly associated with infection or that the resolution of obstruction with PCNL is a vital event in preventing infection.

There are several limitations to this meta-analysis. Heterogeneity in study design limits the significance of these results. Although studies were separated into prospective and retrospective designs, there were many technical aspects that varied between studies. Foremost is the use of SIRS versus fever in defining postoperative infection. Fever in a postoperative setting could be due to pulmonary reasons or other various factors not directly associated with PCNL. Therefore, false positive diagnosis

Previous studies have shown that sex is a risk factor for infection

for ideal management.¹⁷ Previous studies have shown that sex is a risk factor for infection.^{14,18} These studies specifically identified women to be more prone to infection, especially during ureteral catheterization due to poor genital hygiene, cystoceles requiring a pessary, and atrophic vaginitis. However, of the studies investigated, only one identified sex as a significant risk factor. With proper preoperative prepping, these factors associated with ureteral catheterization are assumed to be minimal. No studies in either the retrospective or prospective analyses found age or BMI

staghorn calculi are of larger size; thus these two factors are often linked. Larger and increasingly complex stone configurations often require additional access points, which is a factor significantly associated with postoperative infection

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in both our prospective and retrospective analyses. Increasing stone size could also lead to a higher amount of endotoxin, although this mainly pertains to struvite stones.

of PCNL-related infection in these studies could have led to an overestimation of a factor's significance. Another important variable was the type of prophylactic antibiotic

used in each study. Although a majority of studies used antibiotics in concurrence with the AUA Best Practice Statement on Antimicrobial Prophylaxis, there were three prospective studies and one retrospective study that did not specifically report the antibiotic used. The use of an ineffective antibiotic could lead to increased infection rate and an overestimation of a risk factor's significance. Length of antibiotic use was not described in our study. Most studies used a one-time prophylactic dose at anesthesia induction. However, several studies continued antibiotics postoperatively, often until nephrostomy tube removal. This variable was not expected to influence results, as studies have shown that duration of antibiotic therapy is not significant in preventing sepsis.^{21,22}

Conclusions

Several factors were found to be significantly associated with postoperative infection after PCNL. In both prospective and retrospective studies, preoperative urine culture, stone culture, number of access points, and need for blood transfusion were found to be significant factors. This indicates that the presence of bacteria in the urine/stone

preoperatively, as well as the amount of trauma the kidney sustains during the procedure, are predictors of postoperative infection. We believe that this is the first meta-analysis to identify these risk factors. ■

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MAIN POINTS

- Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure designed to remove large-volume upper urinary tract stones. It is extremely effective yielding high stone-free rates; however, significant complications can occur, including infection.
- Perioperative factors, such as preoperative urine culture, and intraoperative stone and collecting system urine cultures, have been identified as predictors of infection. Intraoperative renal pelvis and stone culture results were the strongest predictors of postoperative infection.
- Perioperative factors, including blood transfusion and number of access points, were found to be significantly associated with infection in both the prospective and retrospective meta-analyses.
- Previous studies have shown that staghorn formation is a risk factor for infection. However, in our analysis, this was only true in retrospective studies. This may be due to stones now predominantly being composed of hydroxyapatite and not struvite.